A time-lapse and quantitative modelling analysis of neural stem cell motion in the absence of directional cues and in electric fields.

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Public Summary:
The authors studied migration of neural stem cell (NSC) migration with time-lapse and quantitative modelling methods. Using time-lapse imaging, the author analyzed the NSC mode of migration. Electric fields suppressed the formation of protrusions oriented toward the anode, suggesting that restriction of protrusions. The authors generated a model of NSC migration with only two key parameters, the probability that a cell will change direction and the probabilities for each of the directions the cell can take. This model can accurately reproduce experimental migration patterns.

Scientific Abstract:
Neural stem cell (NSC) migration is an important component of their developmental function and therapeutic potential. Understanding their mode of migration and their response to guidance cues can contribute to improved therapies for CNS repair, in which appropriate homing to sites of injury is essential. Using time-lapse imaging, we have analyzed the NSC mode of migration in vitro, both in the absence of directional cues and in the presence of applied electric fields (EFs), previously shown to constitute a strong directional signal for these cells. Without EFs, NSCs displayed an amoeboid motion, characterized by small lamellipodial-like protrusions with changing orientations, leading to highly tortuous migration. In EFs, tortuosity diminished as electrotaxis toward the cathode occurred. EFs suppressed the formation of protrusions oriented toward the anode, suggesting that restriction of protrusions with opposing orientation could underlie the change from tortuous motion to directed migration. Treatment with LY294002, a phosphatidylinositol-3-OH kinase (Pi3K) inhibitor, reduced the cathodal bias of protrusions in EFs and the frequency of changes in direction. We generated a model of NSC migration with only two key parameters, which could accurately reproduce experimental migration patterns, and we used it to show that both effects of LY294002 contribute to impair electrotaxis, although decreased protrusion bias is the most important. Our results show that control of protrusion orientation by EFs is an important component of the electrotactic response. A simple modelling approach might be useful in understanding how diverse pharmacological treatments or genetic deletions affect different kinds of directional cell migration.